Atty. Docket No.: 21715/1010 **PATENT**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application of:	Pelletier et al.	Examiner:	Kam, C. M.
Serial No.:	09/689,952		
Filed:	October 12, 2000	Group Art Unit:	1653
Titled:	Compositions and Methods Involving an Essential Staphylococcus Aureus Gene and its Encoded Protein		
		Conf. No.:	7855

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8a

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AFD

DECLARATION OF DR. JERRY PELLETIER

Sir:

I declare that:

1. I am one of the joint inventors of the above identified US patent application. I am also one of the three co-founders of PhageTech Inc., the Assignee.

2. I have been an Associate Professor at McGill University, Montréal, Québec, Canada for 23 years. I am presently Associate Professor at the Department of Oncology, at McGill University. I have worked in the field of genomics and proteomics for at least 25 years. A copy of my CV is attached as **Annex 1**.

3. I have reviewed the specification and the claims of the above-captioned application, as well as the Office Action mailed January 26, 2004 concerning the above-identified application.

4. The following work was performed under my direction or subject to my review, and was performed using the guidance provided in the present specification and routine knowledge in the field.

5. Subsequently to the identification of 77ORF104 (i.e. the bacterial growth inhibitory bacteriophage polypeptide binding to DnaI that is described in the present application), an additional phage polypeptide with similar biological activity to that of 77ORF104 was identified. That additional phage polypeptide is called PVLORF16.

6. Briefly, the genome sequence of bacteriophage PVL was publicly available. The open reading frames (ORFs) of that phage were PCR amplified and cloned into an expression vector. Inhibitory ORFs were identified by dot screening and potential inhibitors were confirmed by growth kinetic studies. PVLORF16 was found to be a cytostatic inhibitor (see **Annex II-A** enclosed herewith). The interaction of PVLORF16 and *S. aureus* DnaI was tested in the yeast two-hybrid system, where PVLORF16 was found to bind to *S. aureus* DnaI when expressed in either direction (i.e. with PVLORF16 in activating domain and DnaI in binding domain, and vice-versa). The effect of PVL16 expression on macromolecular synthesis of *S. aureus* was conducted, and as for 77ORF104, PVLORF16 selectively inhibited DNA synthesis (see **Annex II-B**).

7. Those results confirm that additional bacterial growth inhibitory bacteriophage polypeptide(s) binding to and inhibiting the activity of *S. aureus* DnaI can be readily identified using the method of the present invention.

8. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

Date: April 23rd, 2004

Jerry Pelletier

Dr. Jerry Pelletier

Encl. **Annex 1:** CV of Dr Jerry Pelletier

Annex 2: Figure showing inhibition of *S. aureus* growth by PVLORF16

ANNEX 1 : CV of Dr. Jerry Pelletier

NAME: **Jerry Pelletier**

ACADEMIC DEGREES

1). B.Sc. - Dept. of Biochemistry, McGill University. (1978-1981).
2). Ph. D.- Dept. of Biochemistry, McGill University. (1981-1988).
Supervisor: Dr. Nahum Sonenberg.
Project: Translation Initiation of Eukaryotic Protein Biosynthesis

RESEARCH TRAINING

1988-1991. Post-doctoral Research at the Center for Cancer Research, Department of Biology, Massachusetts Institute of Technology.
Director: Dr. David Housman
Project: Molecular Genetics of Wilms' Tumor

ACADEMIC APPOINTMENTS

1991-1996. Assistant Professor. Dept.. of Biochemistry, McGill University.
1991-1996. Assistant Professor. Dept. of Oncology, McGill Univeristy
1996-present. Associate Professor. Dept. of Biochemistry, McGill University.
1996-present. Associate Professor. Department of Oncology, McGill University.

AWARDS

1991-1996	Medical Research Council of Canada Scholar
1996-2001	Medical Research Council of Canada Scientist
1997	National Cancer Institute of Canada William Rawls Award
2001	Canadian Institues of Health Research Senior Investigator Award

1. RESEARCH SUMMARY

The classic paradigm of drug discovery consists in identifying small molecules capable of modulating the activity of specific protein targets. A comprehensive analysis of the drug targets underlying current drug therapy undertaken in 1996 revealed that present-day therapy addresses only about 500 molecular targets – with cell membrane proteins constituting 45% of all targets and enzymes accounting for 28% of all current drug targets. The promise that genomics research holds for drug discovery lies in the identification of those gene products whose inappropriate expression results in disease. Although, not all of these are likely to constitute feasible drug targets in the classical sense, it is expected that there will be an increase in the number of protein targets that will be exploitable for future drug development. The increasing awareness of the essential role of RNA in many biological processes and in the progression of disease makes it a very attractive therapeutic target. RNA plays an essential role in many macromolecular processes, contains complex secondary and tertiary structural folds, and lacks a cellular repair mechanism. Indeed, the strategy of modulating gene expression by targeting RNA has spawned several new classes of rational designed therapeutics (such as ribozymes, DNAzymes, and antisense oligonucleotides), but to date, these technologies have had very limited clinical success. The major reason for this being the difficult pharmacological barriers these macromolecules must overcome. However, the ability of small molecules to interact with RNA is well known, and

these interactions have the potential to prevent or enhance gene expression, achieve allele-specific modulation of gene expression (when allelic sequence differences result in altered RNA conformations, achieve isoform-specific modulation of gene expression, and exhibit allosteric effects. Our understanding of the binding properties of RNA have come essentially from three areas: (i) analyzing the three dimensional structure of RNA complexed with small molecules (such as antibiotics); (ii) defining the binding properties/requirements of RNA and ligand obtained from *in vitro* SELEX (Systematic Evolution of Ligands by Exponential Enrichment) experiments; and (iii) understanding the manner in which RNA and proteins interact. We have begun a research program in which we are attempting to modulate gene expression by targeting mRNA with small molecule inhibitors. Targeting mRNA provides several advantages not affordable by targeting the corresponding protein product. Our strategy consists of developing bivalent compounds (chemical inducers of dimerization [CID]) that would induce a cooperative interaction between a protein and a specific mRNA target. Formation of stable, high affinity protein/mRNA complexes is expected to interdict gene expression by inhibiting mRNA translation - a well characterized process known to have several facets of regulation and not widely appreciated for drug targeting.

We are interested in applying the tool of chemical genomics to dissect and elucidate the process of eukaryotic protein synthesis. Small molecule ligands, acting as inhibitors, have provided formidable insight into the complexity of prokaryotic translation. We propose that similar inhibitors of eukaryotic translation would be valuable tools to better understand the intricacies and regulation of this pathway. Moreover, only from a more complete picture of eukaryotic protein synthesis can one obtain the necessary means to design therapies that target translation to treat disease. Consequently, we have established a research program aimed at identifying inhibitors of mammalian protein synthesis, elucidating their mode of action, and identify their molecular targets.

PUBLICATIONS

A) Peer Reviewed, Published and In Press

1. Pelletier, J. and N. Sonenberg. (1985). Insertion Mutagenesis to Increase Secondary Structure Within the 5' Noncoding Region of a Eukaryotic mRNA Reduces Translational Efficiency. *Cell* **40:** 515-526.

2. Darveau, A., J. Pelletier, and N. Sonenberg. (1985). Differential Efficiences of In Vitro Translation of Mouse c-myc Transcripts Differing in the 5' Untranslated Region. *Proc. Natl. Acad. Sci. USA* **82:** 2315-2319.

3. Sarkar, G., J. Pelletier, R. Bassel-Duby, A. Jayasuriya, B.N. Fields, and N. Sonenberg. (1985). Identification of a new Polypeptide Coded by Reovirus Gene S1. *J. Virol.* **54:** 720-725.

4. Pelletier, J. and N. Sonenberg. (1985). Photochemical Crosslinking of Cap Binding Proteins to Eukaryotic mRNAs: Effect of mRNA 5' Secondary Structure. *Mol. Cell. Biol.* **5:** 3222-3230.

5. Pelletier, J., R. Nicholson, R. Bassel-Duby, B.N. Fields, and N. Sonenberg. (1987). Expression of Reovirus Type 3 (Dearing Strain) sigma 1 and sigma s Polypeptides in Escherichia coli. *J. Gen. Virol.* **68:** 135-145.

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88. Liu, J., Dehbi, M., Moeck, G., Arhin, F., Bauda, P., Bergeron, D., Callejo, M., Ferretti, V., Ha, N., Kwan, T., McCarty, J., Srikumar, R., Williams, D., Wu, J., Gros, P., Pelletier, J., and DuBow, M. (2003) Antimicrobial drug discovery from bacteriophage genomics. **Submitted.**

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90. Itoh, A., Tanahashi, T., Nagakura, N., Takenaka, Y., Chen, C.-C., Pelletier, J. (2003). Flavonoid glycosides from *Adina racemosa* and their inhibitory properties on eukaryotic protein synthesis. *J. Natl. Prod.* **Submitted**.

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B) Book Chapters and Reviews

1. Sonenberg, N., I. Edery, G. Sarkar, and J. Pelletier. (1986). Eukaryotic mRNA Cap Binding Protein Complex and 5' mRNA Secondary Structure: Studies in Uninfected and Poliovirus-Infected Cells. In "*Current Communications. Molecular Biology - Translational Control.*" (Mathews, M.B., ed.) Cold Spring Harbor Laboratory, New York pp. 30-34.

2. Pelletier, J. and N. Sonenberg. (1987). The Involvement of mRNA Secondary Structure in Protein Synthesis. *Biochem. Cell. Biol.* **65:** 576-581.

3. Edery, I., J. Pelletier, and N. Sonenberg. (1987). Role of Eukaryotic RNA Cap-Binding Protein in Regulation of Translation. In "*Translational Regulation of Gene Expression.*" (Ilan, J., ed.) Plenum Press, New York, pp. 335-366.

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7. Pelletier, J., Munroe, D., and Housman, D.(1991). Molecular Genetics of Wilms' Tumor. In 'Genome Analysis Vol 3: Genes & Phenotypes'. Cold Spring Harbor Laboratory Press, N.Y. pp 135-169.

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10. Bruening, W. and Pelletier, J. (1994) Denys-Drash syndrome: A role for the WT1 tumor suppressor gene in urogenital development. *Seminars in Developmental Biology* **5:** 333-343.

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12. Bardeesy, N. and Pelletier, J. (1995) Mutational Detection by Single Strand Conformational Polymorphism. In "PCR in Neuroscience." (G. Sarkar, ed.) [Academic Press, New York] p.163-183.

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C) Abstracts and Presentations

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21. Haber, D., A. Buckler, K. Call, J. Pelletier, and D. Housman. (1990). Description of a 25 bp Deletion Within the Wilms' Tumor Gene. UCLA Symposium on Negative Controls of Cell Growth. Taos, New Mexico.

22. Buckler A., J. Pelletier, D. Haber, K. Call, and D. Housman. (1990). Isolation and Developmental expression of a murine cDNA Homologous to the Human Wilms' Tumor Gene. UCLA Symposium on Negative Controls of Cell Growth. Taos, New Mexico.

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27. Pelletier, J. (1992). Germline mutations in the Wilms' tumor suppressor gene (WT1) associated with Denys-Drash Syndrome. International Pediatric Nephrologists Association. Jerusalem, Israel. Aug. 31-Sept.4.

28. Pelletier, J. and Bruening, W. (1992). WT1 Mutations and Denys-Drash Syndrome. The 3rd Annual Human Chromosome 11 Meeting. San Diego. California. Sept. 13-Sept. 16.

29. Pelletier, J. and Bruening, W. (1992). WT1 Mutations and Denys-Drash Syndrome. The 42nd Annual Meeting of the American Society of Human Genetics. November 9-13,1992.

30. Pelletier, J. (1993). WT1 Mutations Associated with Abnormal Urogenital Development. Oncogenes and antioncogenes in differentiation, development, and human cancer. American Association for Cancer Research, Inc. Montana, Feb. 1-6.

31. Pelletier, J. (1993). Mutations in the Wilms' tumor suppressor gene, WT1, associated with abnormal growth and development. 5th Annual Meeting of the Society for Human Genetics.March 17-20, Wurzburg, Germany.

32. Mundlos, S., Pelletier, J., and Zabel, B. (1993) Role of Wilms' Tumor Gene WT1 in the Development of Human Urogenital System - Localization of WT1-mRNA and Protein in Developing Human Tissues. 5th Annual Meeting of the Society for Human Genetics.March 17-20, Wurzburg, Germany.

33. Machin, G., Idikio, H., and Pelletier, J. (1993) Atypical Clinical Presentation of Denys-Drash Syndrome in a Female with a Novel WT1 Gene Mutation. 3rd International Workshop on Fetal Genetic Pathology. Perugia, Italy. June 3-6.

34. Pelletier, J. (1993) WT1 Mutations and Urogenital Development. New Directions in Cancer Research. A Symposium in Honour of Peter G. Scholefield. Honey Harbour. Ontario, Canada. Sept. 19-22.

34. Coppes, M.J., Pelletier, J., and Huff, V. (1993) Constitutional WT1 Mutations: An Additional Diagnostic Criterion for the Denys-Drash Syndrome. International Society of Pediatric Oncology. XXVth Meeting. October 5-9. San Francisco.

35. Varanasi, R., Bardeesy, N., Ghahremani, M., Petruzzi, M.J., Nowak, N., Shows, T., and Pelletier, J. (1993) Fine Structure Analysis of the WT1 Gene in Sporadic Wilms' Tumors. American Society of Human Genetics. New Orleans.

36. Bardeesy, N., Falkoff, D., Petruzzi, M.-J., Zabel, B., Nowak, N.,Shows, T., and Pelletier, J. (1994) P53 Mutations Associated with Anaplastic Wilms' Tumor, A Histological Subtype with Poor Prognosis. February 13-20, Keystone Symposium on Tumor Suppressor Genes, Taos, New Mexico.

37. Bruening, W. and Pelletier, J. Alternative Translational Initiation of the WT1 Tumor Suppressor Protein. (1994) 85th Annual Meeting of the American Association for Cancer Research. April 10-13, 1994 San Francisco, California.

38. Diller, L., Drefus, M.G., Li, F.E. and Pelletier, J. (1994) Constitutional mutations of the WT1 gene in patients with Wilms' tumor (WT) and genitourinary (GU) anomalies. American Society of Clinical Oncology.

39. Pelletier, J. (1994). WT1 Mutations and Denys-Drash syndrome. Genetics Society of Canada/Canadian Society for Plant Molecular Biology. Edmonton, Alberta. June 8-11.

40. Lowe, S.W., Bodis, S., Bardeesy, N., McClapchey, A., Remington, L., Ruley, H.E., Fischer, D.E., Jacks, T., Pelletier, J., and Housman, J. (1994) Apoptosis and the prognostic significance of p53 Mutations. Cold Spring Harbor Symposia on Quantitative Biology.

41. Pelletier, J., Beckwith, B., and Bardeesy, N. (1994) Clonal Expansion to Anaplasia in Wilms' Tumors is Associated with p53 Mutations. American Society for Human Genetics. Montreal, Quebec, Canada, October 20, 1994.

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43. P.R. Goodyer, E. Torban, M. Dehbi, J. Pelletier. (1994) Transcriptional regulation of human retinoic acid receptor-alpha (RAR-α) by Wilms' tumor gene product, wt1. American Society for Human Genetics. Montreal, Quebec, Canada, October 20, 1994.

44. N. Bardeesy, P. Mofett, W. Bruening, and J. Pelletier. (1995) The Genetics of Wilms' tumor: An Intersection between Oncogenesis and Development. "Signal Transduction of Normal and Tumor Cells". AACR Special Conference, Alberta, Canada. April 1-6.

45. Pelletier, J. (1995) Rapid Identification and mapping of transcription initiation sites. CGAT Meeting, Toronto, April 6-9th.

46. E. Ferretti, E. Torban, C. Goodyer, J. Pelletier, P. Goodyer (1995) Growth factor-receptor interaction in proliferation and differentiation. Xth Congress of the International Pediatric Nephrology Association. Santiago, Chile.

47. D.J. Munroe, E. Bric, J. Pelletier, S. Morgenbesser, D. Prawitt, R. Loebbert, S. Sait, N. Nowak, M. Higgins, M.J. Petruzzi, S. Dasgupta, A. Winterpacht, B.U. Zabel, T.B. Shows, A.

Buckler, and D.E. Housman (1995) A small region on 11p15.5 that is homozygously deleted in Wilms' tumors. 45th annual meeting of the American Society of Human Genetics.

48. D.J. Munroe, Pelletier, J., Morgenbesser, S., Bric, E., Prawitt, D., Chu, L.L., Zuo, L., Landers, J., Nowak, ., Petruzzi, M.J., Weiss, R., Sait, S., Davis, C., Dasgupta, S., Loebbert, R., Whitton, T., Buckler, A., Catchpole, D., Maher, E., Winterpacht, A., Zabel, B.U., Evans, G., Shows, T.B., and Housman, D.E. (1996) Homozygous deletions in Wilms' tumors localize the WT2 gene. 46th annual meeting of the American Society of Human Genetics. San Francisco.

49. Prawitt, D., Munroe, D.J., Pelletier, J., Loebbert, R., Bric, E., Hermanns, P., Housman, D.E., Winterpacht, A., and Zabel, B.U. (1996). Identification of a NAP related gene in the Wilms' tumor candidate region at 11p15.5. 46th annual meeting of the American Society of Human Genetics. San Francisco.

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51. Moffett, P., Dayo, P., Reece, M., McCormick, M.K., and Pelletier, J. (1996). Isolation and molecular characterization of a mammalian homologue of the drosophila sim transcription factor. 46th Meeting of the American Society of Human Genetics. San Francisco. Oct. 29th-Nov. 2.

52. Moffett, P., Reece, M., and Pelletier, J. (1997). The murine sim-2 gene product inhibits transcription by active repression and functional interference. American Association for Cancer Research. "Transcriptional Control of Proliferation, Differentiation, and Development." Lake George, New York. Oct. 17-Oct. 21.

53. Kim, J., Lee, K., and Pelletier, J. (1997). Characterization of EWS/WT1 fusion proteins and their role in Desmoplastic Small Round Cell Tumor. American Association for Cancer Research. "Tumor Suppressor Genes" Victoria, British Columbia. Sept. 26-Sept. 29.

54. Prawitt, D., Gaertner, B., Higgins, M., Shows, T.B., Pelletier, J., Winterpacht, A. and Zabel, B. (1997). Characterization of transcripts expressed in kidney and derived from 11p15.5, a region linked to Beckwith-Wiedemann syndrome and Wilms' tumor formation. 47th Meeting of the American Society for Human Genetics.

55. Discenza, M., Dehbi, M., and Pelletier, J. (1998). Identification of a novel binding activity with specificity for the wt1 tumour suppressor gene promoter. Cancer Genetics & Tumour Suppressor Genes. Cold Spring Harbor Laboratory. Aug. 19-23.

56. Kim, J., Prawitt, D., Zabel, B., and Pelletier, J. (1998). Involvement of the WT1 tumor suppressor gene in urogenital system development. Cancer Genetics & Tumour Suppressor Genes. Cold Spring Harbor Laboratory. Aug. 19-23.

57. Pelletier, J. (1998) Full-length cDNA cloning: A workshop on problems and solutions. The Banbury Center, Cold Spring Harbor Laboratories. March 23-25.

58. Discenza, M.T. and Pelletier, J. (2000) Identification of a Pea3 responsive element in the WT1 tumour supressor gene promoter. 50th Annual Meeting of the American Society of Human Genetics. Philadelphia, Pennsylvania. Oct. 3 – Oct. 7, 2000.

59. Discenza, M.T., Chu, L.L., Eclees, M., and Pelletier, J. (2002). Renal Hypoplasia in mice heterozygous mutant for WT1 and Pax2. Cold Spring Harbor Mouse Molecular Genetics Meeting. Cold Spring Harbor Laboratory. Aug. 28th-Sept. 1, 2002.

60. Park, E.-H., Lee, J.M., and J. Pelletier (2002). Structure/function relationships of the uORFs within the 5' untranslated region of the human Tie-2 mRNA. Translational Control. Cold Spring Harbor Laboratory. Sept. 10th-Sept. 15, 2002.

61. Moeck, G., Arhin, F., Bauda, P., Bergeron, D., Dehbi, M., Ferretti, V., Ha, N., Kwan, T., Liu, J., McCarty, J., DuBow, M., Gros, P., and Pelletier, J. Integration of Phage Genomics With Target Identification and HTS- A Novel Approach to Drug Discovery. Society for Biomolecular Screening. 8th Annual Conference. Sept. 22-26, 2002.

61. Liu, J., Dehbi, M., Moeck, G., Arhin, F., Bauda, P., Bergeron, D., Callejo, M., Ferretti, V., Ha, N., Kwan, T., McCarty, J., Srikumar, R., Williams, D., Wu, J., Gros, P., Pelletier, J., and DuBow[2w,] M. Impact of bacteriophage genomics on target identification and validation for antibacterial discovery. Society for Biomolecular Screening. 2003 SBS Annual Conference. Portland, Oregon. Sept. 21-25th, 2003.

- **Invited Presentations at International Meetings**

-The 2nd Eastern Canadian Conference on Cancer and Development. "Role of the Wilms' tumor suppressor gene in urogenital development." Montreal. Quebec. (September 1991)
- International Pediatric Nephrologists Association. "Germline mutations in the Wilms' tumor suppressor gene (WT1) associated with Denys-Drash Syndrome." Jerusalem, Israel. Aug. 31-Sept.4, 1992.
- American Association for Cancer Research. International Meeting on Oncogenes and Antioncogenes in Differentiation, Development, and Human Cancer. "WT1 Mutations Associated with Abnormal Urogenital Development." Montana. USA. Feb. 6, 1993.
- The 5th Annual Meeting of the Society for Human Genetics. "Mutations in the Wilms' tumor suppressor gene, WT1, associated with abnormal growth and development." Wurzburg, Germany. March 17-20, 1993
- Honey Harbor Symposium. "WT1 Mutations and Urogenital Development." Honey Harbor, Ontario. Sept. 20, 1993.
- The Genetics Society of Canada/ Canadian Society for Plant Molecular Biology. "WT1 mutations and Denys-Drash syndrome." Edmonton, Alberta. June 1994.
- American Association for Cancer Research - Special Conference on Signal Transduction of Normal and Tumor Cells. "The Genetics of Wilms' tumor: An Intersection between Oncogenesis and Development." Alberta, Canada. April 3, 1995.

- Canadian Genome And Technology Annual Meeting. "Rapid Identification and mapping of transcription initiation sites." Toronto. April 6-9th, 1995.
- The Royal College of Physicians and Surgeons of Canada. "Molecular Genetics of Wilms' Tumor". Montreal. Sept. 15, 1995.
- Sequana Inc., San Diego. (Dr. Alan Buckler - host) "Use of CAPture to isolate full-coding cDNA sequences". May 1997.
- NIH, National Cancer Institute. (Dr. Robert Strausberg – host) "Use of CAPture to isolate full-coding cDNA sequences". May 1997.
- Banbury Meeting at CSH on Full-length cDNA Cloning: Workshop on Problems and Solutions. Cold Spring Harbor Laboratory, March 1998.
- Variagenics Inc., Boston, MA. (Dr. Vincent Stanton – host) "Improvements in full-length cDNA cloning". July 1999.

- **Invited Presentations at Academic Institutions**

- May 1991. "Molecular Genetics of Wilms' Tumor." London Regional Cancer Center, London, Ontario.
- May 1991. "Cloning and Characterization of the WT1 tumor suppressor gene." McGill Cancer Center, McGill University, Montreal.
- March 1992 "Characterization of the WT1 Tumor Suppressor Gene." Department of Biochemistry. McGill University, Montreal.
- Feburary 25, 1992 "Characterization of the WT1 Tumor Suppressor Gene." Lady Davis Bloomsfield Lecture Hall, Jewish General Hospital.
- Feb. 28, 1992 "Characterization of the WT1 Tumor Suppressor Gene." Montreal Childrens' Hospital, Montreal.
- April 15, 1992 "The role of the WT1 Tumor Suppressor Gene in Urogenital Development." Royal Victoria Hospital.
- May 25, 1992 "The role of the WT1 Tumor Suppressor Gene in Urogenital Development." Montreal Childrens' Hospital, Montreal.
- Nov. 26, 1992 "The role of the WT1 Tumor Suppressor Gene in Urogenital Development." Royal Victoria Hospital - Primrose Lecture Series.
- April 16, 1993 "Molecular Genetics of Wilms' Tumor." Sherbrooke University, Dept. of Microbiology.
- March 28, 1994. "Genetics of Wilms' Tumor. Montreal General Hospital." McGill Centre for Host Resistance. Montreal General Hospital, Montreal.
- May 1994. "Genetic Catastrophies in Wilms' tumors." Dept. of Biochemistry, McGill University.
- Nov. 30, 1994 "Genetic Catastrophies in Wilms' tumors." Montreal Cancer Institute, Notre-Dame Hospital. Montreal.
- Feb. 9, 1995. "Molecular Genetics of Wilms' Tumor." Division of Nephrology, Royal Victoria Hospital. Montreal.
- March 20, 1995. "Molecular Genetics of Wilms tumors: Rare insights into normal and abnormal renal development." MacMaster University.
- March 21, 1995. "Molecular Genetics of Wilms tumors: Rare insights into normal and abnormal renal development." York University.

- March 24, 1995. "Molecular Genetics of Wilms tumors: Rare insights into normal and abnormal renal development." Dept. Med. Genetics. Montreal Childrens' Hospital.
- Nov., 1997. "Molecular Genetics of Wilms tumors: Rare insights into normal and abnormal renal development." William Rawls Acceptance Lecture. McGill University.

FUNDS HELD FOR RESEARCH OPERATION
(excepted for when noted, I was principle and sole investigator on these grants)

Support Period: 1991 Amount/yr: $46,020
Agency: NCIC – Terry Fox Equipment Grant
Title: Characterization of the Wilms tumor gene promoter and mapping of the second WT locus.

Support Period: 1991-1994 Amount/yr: $74,620
Agency: NCIC
Title: Characterization of the Wilms tumor gene promoter and mapping of the second WT locus.

Support Period: 1991-1994 Amount/yr: $78,838
Agency: MRC
Title: Involvement of the WT1 gene in genitourinary development

Support Period: 1992-1994 Amount/yr: $40,000
Agency: Kidney Foundation of Canada (KFOC)
Title: Role of the Wilms tumor gene in kidney development

Support Period: 1992-1995 Amount/yr: $42,998
Agency: NIH Subcontract
Title: Molecular Epidemiology of Wilms' tumor
*I was co-applicant on this grant and the Principle Investigator was Dr. Fred Li (Dana Farber Cancer Research Center).

Support Period: 1993-1996 Amount/yr: $99,295
Agency: Canadian Genome Analysis & Technology Program (CGAT)
Title: Rapid identification and mapping of transcription initiation sites

Support Period: 1994-1996 Amount/yr: $40,000
Agency: KFOC
Title: In Vivo downstream targets of the Wilms' tumor suppressor gene product

Support Period: 1994-1997 Amount/yr: $88,000
Agency: NCIC
Title: Structure-function relationships of the WT1 and p53 tumor suppressor genes in WTs.

Support Period: 1994-1997 Amount/yr: $70,000
Agency: MRC
Title: Post-transcriptional regulation of the WT1 tumor suppressor gene.

Support Period: 1995-1998 Amount/yr: $130,000
Agency: CGAT
Title: Generation of 5' anchor sites for transcript mapping

Support Period: 1996-1998 Amount/yr: $40,000
Agency: KFOC
Title: Regulation of WT1 gene expression.

Support Period: 1997-2000 Amount/yr: $103,042
Agency: NCIC
Title: Characterization of interstitial deletions in Wilms' tumor

Support Period: 1997-2000 Amount/yr: $81,345
Agency: MRC
Title: Structure-function analysis of the WT1 tumor suppressor gene

Support Period: 1998-2000 Amount/yr: $135,000 USD
Agency: Merck Genome Research Initiative
Title: Generation of Full-length cDNA libraries for facilitating gene discovery

Support Period: 1998-2000 Amount/yr: $40,000
Agency: KFOC
Title: Characterization of the WT1 regulatory pathway

Support Period: 1999-2002 Amount/yr: $180,000 USD
Agency: NIH
Title: Improved technologies for full-length cDNA generation.

Support Period: 2000-2001 Amount/yr: ~$90,000
Agency: Valorisation Quebec (VRQ)
Title:
*I was co-applicant on this grant and the Principle Investigator was Dr. Michael Tremblay (McGill University).

Support Period: 2000-2005 Amount/yr: $121,662
Agency: MRC
Title: Structure-function relationship of the EWS/WT1 oncogene.

Support Period: 2000-2005 Amount/yr: $138,528
Agency: NCIC
Title: Downstream targets of the WT1 tumor suppressor gene product.

Support Period: 2000-2003 Amount: $1,000,000/3 yrs
Agency: NCIC

Title: Novel approaches for targeting RNA with small molecules.

Support Period: 2002-2005 Amount: $268,000/yr
Agency: VRQ
Title: The Quebec Combinatorial Chemistry Consortium.

Support Period: 2002-2004 Amount: $60,000/yr
Agency: Hereditary Disease Foundation (USA)
Title: Targeting the translation of the huntingtin mRNA with small molecules.

Support Period: 2003-2006 Amount: $360,000/3 yrs
Agency: NCIC
Title: Chemical Dissection of Eukaryotic Protein Synthesis.

- **Patents**

US2002082394 LOCALIZATION AND CHARACTERIZATION OF THE WILMS' TUMOR GENE

Darveau, A., Bruening, W., Pelletier, J., Ito, C., Buckler, A., Glaser, T., Haber, D., Housman, D., Rose, E., Call, K.

WO0020630 OLIGONUCLEOTIDE PRIMERS THAT DESTABILIZE NON-SPECIFIC DUPLEX FORMATION AND USES THEREOF

Pelletier, J

WO0070039 METHOD FOR SUBTRACTING cDNAs BY SUPPRESSING THE SYNTHESIS OF SPECIFICALLY TARGETED mRNAs

Pelletier, J

WO0055307 A METHOD FOR INCREASING THE PROCESSIVITY OF A DNA- OR RNA-DEPENDENT POLYMERASE AND COMPOSITIONS THEREFOR

Pelletier, J

WO0146383 COMPOSITIONS AND METHODS INVOLVING AN ESSENTIAL STAPHYLOCOCCUS AUREUS GENE AND ITS ENCODED PROTEIN.

DuBow, M., Gros, P., and Pelletier, J.

WO0250545 COMPOSITIONS AND METHODS INVOLVING AN ESSENTIAL STAPHYLOCOCCUS AUREUS GENE AND ITS ENCODED PROTEIN STAAU_R9.

DuBow, M., Gros, P., and Pelletier, J.

WO0250106 COMPOSITIONS AND METHODS INVOLVING AN ESSENTIAL STAPHYLOCOCCUS AUREUS GENE AND ITS ENCODED PROTEIN STAAU_R4.

DuBow, M., Gros, P., and Pelletier, J.

WO0244718 COMPOSITIONS AND METHODS INVOLVING AN ESSENTIAL STAPHYLOCOCCUS AUREUS GENE AND ITS ENCODED PROTEIN STAAU_R2.

DuBow, M., Gros, P., and Pelletier, J.

WO0032825 DEVELOPMENT OF NOVEL ANTI-MICROBIAL AGENTS BASED ON BACTERIOPHAGE GENOMICS

DuBow, M., Gros, P., and Pelletier, J.

- **Reviewer for Scientific Journals**

Nature Genetics
Cell, Growth and Development
Human Molecular Genetics
Molecular and Cellular Biology
EMBO Journal
Genomics
PNAS

- **External Reviewer for Granting Agencies**

-CGAT
-Alberta Heritage Foundation for Medical Research (1994)
-Dutch Cancer Institute (1994)
-CIHR (1992-Present)
-NCIC (1993-Present)

- **Associate Editor for *Physiological Genomics*. (1999 – present).**

Physiological Genomics is an on-line journal supported by the American Physiological Society aimed at publishing the results of a wide variety of studies from human and from informative model systems with techniques linking genes and pathways to physiology, from prokaryotes to eukaryotes. The journal is interested in research that links genes to cell replication, development, metabolic function, cell signal transduction and intracellular signaling pathways, tissue and organ function, and whole organism function. As an associate editor, I handle 3 papers a month for the journal – assigning reviewers, evaluating reviews and communicating with the authors regarding their revisions.

2. TEACHING

- ***Biochemistry 507-460A (Fall 2000)***

Course Coordinator.

[6 credits; enrollment limited] This course is a third year undergraduate laboratory course offered to biochemistry honors and majors students with a minimum CGPA of 3.2. Yearly enrollment has varied between 25-46 students/year (28 students in 2000). This course is divided into three sections. All students perform a common, 2 week long laboratory project under my direct supervision in which they over-express a recombinant protein, purify the protein of interest, and assess its activity in a functional assay. Students then rotate through one of the laboratories in the department, performing a one-month research project under the supervision of a member of that laboratory. Each student will also write a research/review paper on a chosen topic with the guidance of a member of the Biochemistry Dept.

I am aided by two teaching assistants for the common rotation. My direct contact hours with the undergraduate students during these first two weeks are (at a minimum) 6 hours per day, therefore direct contact teaching hours are 60 hours/Fall term for this laboratory. I also correct all individual laboratory reports for this first rotation.

- ***Biochemistry 507-491B (Winter 2002)***

This is a third year lab course in which individual students work on a project performed in a research laboratory for the entire semester. The students that perform this course in my laboratory have generally worked on research programs involving the WT1 tumor suppressor gene. Because the research topic is current, I can spend between 30 min/ week discussing their results to several hours/week showing them new techniques. On average, I would estimate that I spend about 15 hrs/term of direct contact teaching hours.

Winter 2000. Student: Jenny Chan
Project: Characterization of Novel Protein Synthesis Inhibitors

- ***Graduate Student Training***

I have had on average approximately 4-5 graduate students/year in my laboratory. I spend approximately three hours/week with each student. The students which have been in my laboratory during the 2000-2001 year are listed below.

Jungho Kim 1995-2000
Subject: Involvement of WT1 tumor suppressor gene in desmoplastic small round cell tumor
Shelly Lwu 1998-2000
Subject: Isolation and identification of a novel putative WT1-interacting protein
Taeho Lee 1997-2003
Subject: Characterization of a novel putative WT1-interacting protein
Maria Discenza 1994- 2003
Subject: Structure-function analysis of the WT1 promoter.
AbbA Malina 2002- Present
Subject: Characterization of Novel Protein Synthesis Inhibitors.
Eun-Hee Park 2000-Present
Subject: Structure-Function Relationships of the 5' UTR of the Tie-2 gene – Insights into angiogenesis.
Marie-Eve Bordeleau 2002-Present
Subject: Inhibiting Translation Initiation as a Chemotherapeutic Approach
John Mills 2003-Present.
Subject: Molecular Genetics of Lymphomas.

Post-Doctoral Training
Joseph Lee 2003-Present
Subject: A High Throughput Screen for novel inhibitors of cap-dependent initiation.
Shakila Khan 2002-Present
Subject: Phyllanthoside – A novel inhibitor of Eukaryotic Protein Synthesis Elongation.
Olivia Novac 2002-Present
Subject: High Throughput Screening of Novel Inhibitors of Protein Synthesis.

3. ADMINSITRATIVE CONTRIBUTIONS

- **Co-ordinator for Genome Quebec Mouse Functional Genomics Application.**

I was the coordinator for a mutli-disciplinary proposal assembled last year on mouse functional genomics for submission to Genome Quebec. This project was to form part of a larger functional genomics program aimed at integrating studies on yeast, Drosophila, and mouse. It was expected that this integrated program would bring into McGill University ~ $1,200,000 of operational research support, of which ~$600,000 would be earmarked for the McInytre Mouse Functional Genomics Effort.

- **Member of Chemic Biology Studentship Evaluation Panel. Also involved in organization of seminar speakers for chemical biology.**

- **Involved in Organizing and writing CFI grant application for the chemical biology component of the BLSB (Bellini Life Science Building) grant.**

- **Co-Founder and Co-director of the McGill University High Throughput Chemical Screening Facility. (see http://www.medicine.mcgill.ca/biochem/htsfacility/).**

- **Co-Organizer (with Dr. Kalle Gehring) for Meeting on Chemical Genomics/Structural Biology held April 17-18th (2003) at the Holiday Inn (Montreal).**

- **University Committees**

-Grants Review committee for the Research Institute of the Royal Victoria Hospital (Dec. 3, 1992).
-Faculty of Science Committee on Computing (1992-1994)
-Faculty of Graduate Studies and Research. Faculty Council (1992-1996)
-Promotion Committee for Dr. M. Hadjopoulos (Nov. 1994)
-Committee for the re-appointment of Dr. Alan Nepveu to the Dept. of Oncology (Dec. 1994).
-Fellowship Review Committee for Canderel-FCAR Studentships [McGill Cancer Center] (1994-1995). This committee evaluates studentships and post-doctoral fellowship applications from first year applicants.
-McKinnell Travel Grant Review Committee [Dept. Biochemistry] (1994-Present). This committee evaluates abstract proposals and awards travel grants to students to attend meetings.
-Chair of the Graduate Advisory Committee (GAC) of the Dept. Biochemistry (Spring 1997)
-Chair of the Graduate Advisory Committee (GAC) of the Dept. Biochemistry (Fall 2000).
-Member of the Graduate Advisory Committee (GAC) (2000-present). Involves assessing and ranking applications of new graduate students to the Dept., evaluating junior seminars of M.Sc. students, assessing Ph.D. proposals from graduate students transferring from the M.Sc to the Ph.D. biochemistry program, evaluating senior seminars of Ph.D. students, and evaluating and ranking McGill majors and NSERC fellowship applications of graduate students.

- **Scientific Review Panels**

- Member of NIH Site Visit Panel. MD Anderson Medical Center, Texas (April '92)
  - Scientific Officer 1993 - NCIC Panel F (Jan. 28-29,1993)
  - Scientific Officer 1993 - NCIC Panel F (Jan. 20-21,1994)
- Member - NCIC Panel F (Jan. 1995 - 1997)
- Member - Kidney Foundation of Canada Review Panel (1994 - 1996)
- Ad hoc NIH grant review panel (2003)

- **External Evaluator for Tenure for Dr. Yaacov Frishberg - Chair, Division of Pediatric Nephrology, The Hebrew University of Jerusalem (Feb., 2003)**
- **Student Research Advisory Committes**

Mohini Lutchman	Dr. Guy Rouleau	
Scott McDonald	Dr. Jacques Drouin	
Michael Phelan	Dr. Marc Featherstone	
Patrick Nedellec	Dr. Nicole Beauchemin	
Zbynek Bozdech	Dr. Erwin Schurr	
Jovan Antunovic	Dr. Dr. James Cromlish	
Abdullah Abdullah	Dr. Leonard Pinsky	
Lala Torban	Dr. Paul Goodyer	
Jai Chatterjee	Dr. Ted Meighen	
Greg Cosentino	Dr. Nahum Sonenberg	
Josee Dostie	Dr. Nahum Sonenberg	
Anouk Fortin	Dr. Philippe Gros	
Avak Kahwajian	Dr. Nahum Sonenberg	
Albert Lai	Dr. Phil Branton	
Mathieu Miron	Dr. Nahum Sonenberg	
Nam Sung Moon	Dr. Alan Nepveu	
Anna Moraitis	Dr. Vincent Giguere	
Fakhraddin Naghib Al Hossaini	Dr. Cliff Stanners	
Francis Poulin	Dr. Nahum Sonenberg	
Emmanuelle Querido	Dr. Phil Branton	
Jean-Simon Diallo	Dr. Lee Wall/Ann Marie Mes Masson	2002
Olivie	Dr. Phil Branton	2002
--	Dr. Sophie Roy	2002
David Breckenridge	Dr. Gordon Shore	2002

- **Ph.D. Defense Committees (1993-Present)**

Charles Goyer	March 11, 1993	Supervisor: Nahum Sonenberg
Anthony Blanc	April 26, 1994	Supervisor: Nahum Sonenberg
Nathalie Methot	July 17, 1996	Supervisor: Nahum Sonenberg
Stephen Whalen	Dec. 9, 1996	Supervisor: Phil Branton
Kyle Vogan	April 22, 1998	Supervisor: Philippe Gros
Andrew Craig	June 22, 1998	Supervisor: Nahum Sonenberg

Rob Screaton	Nov. 12, 1998	Supervisor: Cliff Stanners
Samantha Gruenheid	Nov. 30, 1999	Supervisor: Philippe Gros
Greg Cosentino	Jan. 10, 2000	Supervisor: Nahum Sonenberg
Kianoush Khaleghpour	Nov 2, 2000	Supervisor: Nahum Sonenberg
Pascal Lachance	Sept. 19, 2001	Supervisor: Paul Lasko
Anny Fortin	Oct. 18, 2002	Supervisor: Philippe Gros

"Identification and characterization of the genetic component of differential susceptibility to mourse malaria"

Andrea Dawn BRUESCHKE Nov. 15th, 2002 Supervisor: Nahum Sonenberg

"Regulation of translation initiation by the 4EBPs and phosphorylation of elF4E"

Degree: M.Sc.

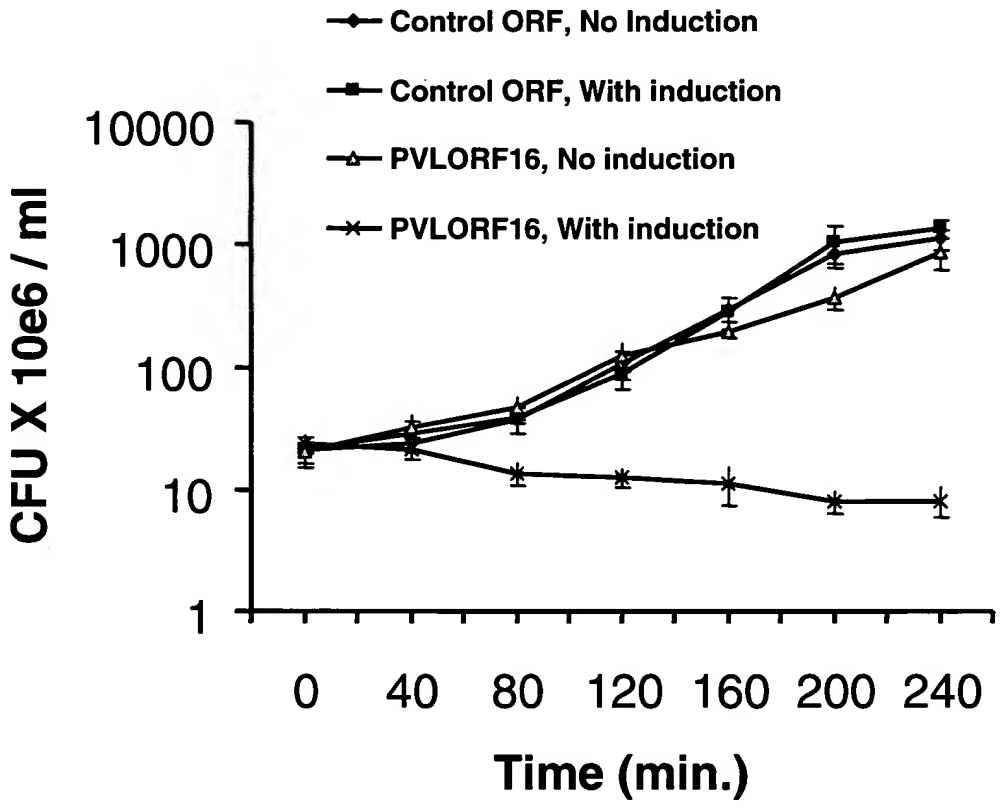
- **Pre-doctoral Exam: Mr. Martin Couillard (April, 2003), IRCM**

- **Co-founder and consultant of PhageTech** (1997-Present). A small start-up Biotech company aimed at discovering novel anti-microbial compounds. The company currently has 19 full-time employees and has a discovery program aimed at identifying drug targets in *Staphylococcus aureus* and *Streptococcus pneumoniae*.

- Co-wrote a Public Awareness Information Sheet for the Kidney Foundation of Canada (KFOC) on Wilms' Tumor (Dec. 1993). This information sheet is provided to parents of children diagnosed with Wilms' tumor to help them understand the disease.
- Consultant – Ardais Scientific Inc. Lexington, MA.
- Member of Merck-Frosst Biohazard Safety Committee

ANNEX 2

A) *S. aureus* growth inhibitory activity of PVLORF16



B) Characteristics of PVLORF16

Origin: *S. aureus* bacteriophage PVL
Size: 297 amino acids
Growth Inhibition: Bacteriostatic
Bacterial target: *S. aureus* DnaI
Binding domain: DnaI amino acids 64-313
Confirmation of binding with target: Yeast two-hybrid (both directions)
Confirmation of Pathway: Specific inhibition of DNA synthesis